



Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

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Pharmacoenhancers

Glossary of Terms for Supplement

Carcinogenic: Producing or tending to produce cancer

- Some agents, such as certain chemicals or forms of radiation, are both mutagenic and clastogenic.
- Genetic mutations and/or chromosomal damage can contribute to cancer formation.

Clastogenic: Causing disruption of or breakages in chromosomes

Genotoxic: Damaging to genetic material such as DNA and chromosomes

Mutagenic: Inducing or capable of inducing genetic mutation

Teratogenic: Interfering with fetal development and resulting in birth defects

Cobicistat (Tybost, COBI)

(Last updated October 26, 2016, last reviewed October 26, 2016)

Cobicistat is classified as Food and Drug Administration Pregnancy Category B.

Animal Studies

Carcinogenicity

At cobicistat exposures 7 times and 16 times the human systemic exposure, no increases in tumor incidence were seen in male and female mice. In rats, an increased incidence of follicular cell adenomas and/or carcinomas in the thyroid gland was observed at doses up to twice the typical human exposure. The follicular cell findings are considered rat-specific, and not relevant to humans.¹

Reproduction/Fertility

No effect has been seen on fertility in male or female rats.¹

Teratogenicity/Developmental Toxicity

Rats and rabbits treated with cobicistat during pregnancy at 1.4 and 3.3 times higher than the recommended human exposure have shown no evidence of teratogenicity.¹

Placental and Breast Milk Passage

No information is available on placental passage of cobicistat. Studies in rats have shown that cobicistat is secreted in breast milk.²

Human Studies in Pregnancy

Pharmacokinetics

Pharmacokinetic studies in pregnancy are limited to a single case report, which found that cobicistat area under the curve was reduced by 44% during the third trimester of pregnancy.³

Placental and Breast Milk Passage

No data are available on placental or breast milk passage of cobicistat in humans.

Teratogenicity/Developmental Toxicity

In the Antiretroviral Pregnancy Registry, no birth defects have been reported in 32 live births with first trimester exposure and 18 live births with second- or third-trimester exposure to cobicistat. The numbers of first-trimester exposures to cobicistat in humans are insufficient to be able to make a risk determination.²

Excerpt from Table 8^a

Generic Name (Abbreviation) Trade Name.	Formulation	Dosing Recommendations	Use in Pregnancy
Cobicistat (COBI) <i>Tybost</i>	<u>Tablet (Tybost):</u> • 150mg	<u>Standard Adult Dose</u> <i>Tybost:</i> • As an alternative PK booster with ATV or DRV: 1 tablet (150 mg) once daily with food.	No data on placental transfer of COBI are available.
Elvitegravir/Cobicistat/ Tenofovir Disoproxil Fumarate/Emtricitabine (EVG/COBI/ TDF/FTC) <i>Stribild</i>	<u>Tablet (Stribild):</u> • EVG 150 mg plus COBI 150 mg plus TDF 300 mg plus FTC 200 mg	<i>Stribild, Genvoya, Evotaz, Prezcobix:</i> • 1 tablet once daily with food.	Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits.
Elvitegravir/Cobicistat/ Tenofovir Alafenamide/ Emtricitabine (EVG/COBI/TAF/FTC) <i>Genvoya</i>	<u>Tablet (Genvoya):</u> • EVG 150 mg plus COBI 150 mg plus TAF 10 mg plus FTC 200 mg	<u>PK in Pregnancy:</u> • No PK studies in human pregnancy.	
Atazanavir/Cobicistat (ATV/COBI) <i>Evotaz</i>	<u>Tablet (Evotaz):</u> • ATV 300 mg plus COBI 150 mg	<u>Dosing in Pregnancy:</u> • Insufficient data to make dosing recommendation.	
Darunavir/Cobicistat (DRV/COBI) <i>Prezcobix</i>	<u>Tablet (Prezcobix):</u> • DRV 800 mg plus COBI 150 mg		

^a Individual antiretroviral drug dosages may need to be adjusted in renal or hepatic insufficiency (for details, see [Adult and Adolescent Antiretroviral Guidelines, Appendix B, Table 7](#)).

Key to Abbreviations: ATV = atazanavir; COBI = cobicistat; DRV = darunavir; EVG = elvitegravir; FTC = emtricitabine; PK = pharmacokinetic; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

References

1. Cobicistat [package insert]. Food and Drug Administration. 2015. Available at http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/203094Orig1s003lbl.pdf. Accessed September 21, 2016.
2. Antiretroviral Pregnancy Registry Steering Committee. Antiretroviral Pregnancy Registry international interim report for 1 January 1989–31 July 2015. Wilmington, NC: Registry Coordinating Center. 2015. Available at <http://www.apregistry.com/>.
3. Schalkwijk S, Colbers A, Konopnicki D, et al. First reported use of elvitegravir and cobicistat during pregnancy. *AIDS*. 2016;30(5):807-808. Available at <http://www.ncbi.nlm.nih.gov/pubmed/26913711>.